

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 6/24/10 has been entered.

2. The supplemental amendment to the claims filed 10/13/10 to include in claim 1 part (b) the phrase "in parallel", which was present in claim 1 as originally filed in the amendment and response dated December 7, 2009, but was inadvertently omitted from the amendment and response dated June 24, 2010 has been entered.

3. Claim 1 has been amended. Claims 10-11 and 18-19 have been cancelled. Claims 1-9, 12-17 and 20 are pending in the application and are under examination.

Priority

4. Receipt is acknowledged of papers filed under 35 U.S.C. 119 (a)-(d) based on an application (GB 0324650.1) filed in Great Britain on 10/22/03. Applicant has not complied with the requirements of 37 CFR 1.63(c), since the oath, declaration or application data sheet does not acknowledge the filing of any foreign application. A new oath, declaration or application data sheet is required in the body of which the present application should be identified by application number and filing date.

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Claim Rejections Withdrawn

5. The rejection of claims 18 and 19 under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement (new matter) is withdrawn in view of the cancellation of the claims.

6. The rejection of claims 1-9 and 12-19 are rejected under 35 U.S.C. 112, second paragraph, is withdrawn in view of the amendment to the claims.

7. The rejection of claims 1-3, 8-9 and 12-18 under 35 U.S.C. 103(a) as being unpatentable over Peck et al. US 5,789,173 Aug. 4 1998, cited previously in view of Kohne et al. US 5,738,988 April. 14, 1998, cited previously is withdrawn in view of the amendment to the claims.

8. The rejection of claims 4-7 under 35 U.S.C. 103(a) as being unpatentable over Peck et al. US 5,789,173 Aug. 4 1998 cited previously and Kohne et al. US 5,738,988 April. 14, 1998 cited previously as applied to claims 1-3, 8-9 and 12-18 above, further in view of Grondhal et al. Journal of Clinical Microbiology, Jan. 1999, p. 1-7 is withdrawn in view of the amendment to the claims.

9. The rejection of claims 4-7 under 35 U.S.C. 103(a) as being unpatentable over Peck et al. US 5,789,173 Aug. 4 1998 cited previously and Kohne et al. US 5,738,988 April. 14, 1998 cited previously as applied to claims 1-3, 8-9 and 12-18 above, further in view of Van Elden et al. The Journal of Clinical Microbiology, Jan. 2001, p. 196-200 is withdrawn in view of the amendment to the claims.

10. The rejection of claims 7, 9 and 19 are rejected under 35 U.S.C. 103(a) as being unpatentable over Peck et al. US 5,789,173 Aug. 4 1998 cited previously and Kohne et al. US 5,738,988 April. 14, 1998 cited previously as applied to claims 1-3, 8-9 and 12-18 above, further in view of De Baere et al. BMC Microbiology March 2, 2002, 2:4 (p. 1- p.12) cited in IDS is withdrawn in view of the amendment to the claims.

***New Rejections Based on Amendment
Claim Objections***

11. Claim 12 is objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form.

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Claim 12 recites "the process of claim 1, wherein the antimicrobial(s) used in step (b) are selected based on the results of step (a). However, the last line of claim 1 already recites "wherein the selected antimicrobials are selected based on the results of step (a). Thus, claim 12 does not further limit the subject matter of claim 1.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

12. Claims 1-7 and 12-17 are rejected under 35 U.S.C. 103(a) as being unpatentable over Peck et al. US 5,789,173 Aug. 4 1998, in view of Remacle et al (WO 01/77372) 10/18, 2001) and Taintor et al (US 2003/0124643 7/3/03).

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Claim 1 and dependent claims are drawn to a process for analyzing a biological sample containing two or more microorganisms, comprising the steps of:

- (a) identifying two or more microorganisms present within the sample by analyzing the two or more microorganisms' nucleic acid; and
- (b) determining, in parallel, the effect of one or more antimicrobial(s) on the two or more different microorganisms in the sample, wherein determining the effect of one or more selected antimicrobials comprises:

- adding an antimicrobial at a plurality of pre-determined concentration to individual aliquots of the sample, wherein one aliquot contains no antibiotic;

- incubating the aliquots for a pre-determined time period under conditions that allow some growth of the two or more microorganisms; and

- assessing the number of each one of the two or more microorganisms in the aliquots at the end of the pre-determined time period by analyzing the microorganisms' nucleic acid;

- wherein steps (a) and (b) are performed by without prior separation of the two or more microorganisms;

- wherein the selected antimicrobials are selected based on the results of step (a).

Peck et al teaches a method for rapid antimicrobial susceptibility comprising: testing to screen the effect of one or more antimicrobials on microbes or microorganisms in biological samples such as human body fluids, blood and other specimens containing microbes without prior separation of microbes or microorganism in the biological sample comprising:

- adding an antimicrobial at a plurality of pre-determined concentration (serial dilution concentration) to individual aliquots of the sample in 96 well plates, wherein one aliquot contains no antibiotic (control column) (see column 3 lines 18-25, lines 47-55, column 7 lines 46-50 and claim 1);

- incubating the aliquots for a short period of time (a predetermined time period) under conditions that allow some growth (incubation for a short time to create differential microbial counts; see column 3 lines 18-26 and claim 1);

- assessing the number of each one of the two or more microorganisms in the aliquots at the end of the predetermined period by analyzing the microorganisms' nucleic acid (amplifying the differential microcounts by in vitro DNA replication ; see column 3 lines 27-28 and claim 1)

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Peck et al teach the process involves polymerase chain reaction which is amplification of nucleic acid from the microorganism and PCR involves a nucleic acid hybridization assay as primers hybridize to the organisms nucleic acid (see abstract and figure 1 “the innovation” and column 2 lines 24-35, 60-67 to column 3 lines 1-7, column 10 claim 1).

Peck et al teach that the differential microbial counts can be amplified by using PCR which involves the use of primers specific to replicate a gene of a microorganism of interest. See column 10 claim 17.

Said method involves analysis of the micro-organism’s DNA e.g. 16s rRNA gene. See column 10 claim 17.

Said microorganism is a bacterium, see for example column 4 lines 59-67, and the antimicrobial is an antibiotic, for example, see column 3 lines 47-55.

Peck et al does not teach identifying the microorganisms (two or more) present in the biological sample by analyzing the microorganisms’ nucleic acid and does not teach that the antimicrobials tested are based on the results of identifying the microorganisms (two or more) present in the biological sample by analyzing the microorganisms' nucleic acid and does not teach identifying the microorganisms (two or more) present within the sample by analyzing the different microorganisms' (two or more) nucleic acid using a probe or a labeled probe.

Remacle teach simultaneous identification of groups or subgroups of microorganisms in the same biological sample by analysis of their nucleic acid using PCR amplification (which involves hybridization of primers or other nucleic acid hybridization assay using capture nucleotide sequence i.e. a probe (p. 1 paragraphs 1-2, p. 6 paragraph 16, p. 8 paragraphs 22-24, p. 8-9 paragraphs 46-47, p. 9 paragraph 50). Remacle teach that said process involves the use of labeled capture sequences (labeled probes). See p. 20 paragraph 70. Remacle et al teach that said method allows the easy identification (detection and/or quantification) of a large number of microorganisms (see p. 5 paragraph 11).

Taintor et al teaches that diagnosis of infectious diseases relies on identification of the microorganism responsible for the infection and then determining the appropriate antimicrobial treatment. Taintor et al teach that the prior art calls for initial identification of the organism first and where a pathogen is identified, performing an antimicrobial susceptibility test. Taintor et al

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teach that the identification of microorganisms and antimicrobial susceptibility can occur at the same time or consecutively. See paragraph 26 on p. 3.

It would have been prima facie obvious to one of ordinary skill in the art at the time the instant invention was made to have modified the method of Peck et al to include a process of identifying two or more different microorganisms present within the biological sample by analyzing the microorganisms' nucleic acid using PCR amplification or nucleic acid hybridization assay using capture nucleotide sequence i.e. a probe or a labeled probe as taught by Remacle et al and selecting the antimicrobials based on the result of said identification, thus resulting in the instant invention with a reasonable expectation of success.

The motivation to do so is because Taintor et al teach that in diagnosis of infectious disease the prior art calls for initial identification of the organism first and where a pathogen is identified, performing an antimicrobial susceptibility which helps to determine the appropriate antimicrobial treatment and in addition, Taintor et al teach that the identification of microorganisms and antimicrobial susceptibility can occur at the same time or consecutively. Furthermore, as to claim 13, comparison of the antimicrobial susceptibility test i.e. step (b) with the identification step of (a) would have been prima facie obvious to one of ordinary skill in the art at the time the instant invention was made to help diagnosis infection i.e. comparing the antimicrobial susceptibility testing results with microorganism identification to determine which pathogens are in the biological sample and thus help determine the proper antimicrobial treatment as taught by Taintor et al.

As to identifying two or more microorganisms by analyzing the microorganisms' nucleic acid using probe or labeled probes (claims 16-17), Remacle et al provides motivation by teaching that simultaneous identification of groups or subgroups of microorganisms in the same biological sample can occur using PCR amplification or using probes or labeled probes.

13. Claims 8 and 9 are rejected under 35 U.S.C. 103(a) as being unpatentable over Peck et al. (US 5,789,173 Aug. 4 1998) and Remacle et al (WO 01/77372 10/18, 2001) and Taintor et al (US 2003/0124643 7/3/03) as applied to claims 1-7 and 12-17 above, further in view of Kohne et al. (US 5,738,988 April. 14, 1998) cited previously.

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The combination of Peck et al and Remacle et al and Taintor et al is set forth supra. Said combination does not teach that the microorganism's RNA is analyzed.

Kohne et al teach a method for detecting, identifying, determining the state of growth and quantitating organisms (e.g. bacteria or viruses) in biological samples (column 11 lines 47-48, column 4 lines 46-49, column 13 lines 10-15) by assessing the number of two or more microorganisms in the sample by analyzing the microorganisms' nucleic acid using probes specific for a particular genus or and another for a different genus (column 12 lines 44-54) or using in lieu of a single probe a multiplicity or battery of different probes wherein each probe is complementary only to the R-RNA or T-RNA of a specific group of organisms and each probe is specific for a different group or organisms, wherein said method is performed without prior separation of the microorganisms. See column 13 lines 34-65 and column 14 lines 35-67 and column 52 claim 20-28. Kohne et al teaches a marker on the probe (labeled probe, column 20 line 46 and column 25 lines 57-60) and teaches an illustrative example of a radioactive probe, (see column 25 lines 40-47, and lines 42-43).

Kohne et al teaches that the detection, identifying and quantitation method can be used to determine the sensitivity of particular groups of organisms including viruses to antimicrobial agents including antiviral agents. See abstract and column 42 lines 6-41 and column 45 lines 45-62.

It would have been prima facie obvious to one of ordinary skill in the art at the time the instant invention was made to have modified the method of Peck et al and Remacle et al and Taintor et al as combined to analyze the microorganisms' RNA as taught by Kohne et al, thus resulting in the instant invention with a reasonable expectation of success. The motivation to do so is that Kohne et al teach that analysis of the RNA of different group or different organisms can be used to detect, identify and determine the state of growth and also that the detection, identifying and quantifying method can be used to determine the sensitivity of particular groups of organisms to antimicrobial agents.

14. Claim 20 is rejected under 35 U.S.C. 103(a) as being unpatentable over Peck et al. (US 5,789,173 Aug. 4 1998) and Remacle et al (WO 01/77372 10/18, 2001) and Taintor et al

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(US 2003/0124643 7/3/03) as applied to claims 1-7 and 12-17 above, further in view of Gorbach et al, Ed. Infectious Diseases, 3rd edition, 2003, Lippincott Williams and Wilkins, Chapter 12, p. 126 and p.142.

The combination of Peck et al and Remacle et al and Taintor et al is set forth supra. Said combination does not teach that said method further comprises assessing by DNA detection the number of one or more microorganisms in an aliquot at a plurality of time points within the pre-determined period.

Gorbach et al teach that a time kill curve is a research tool that is used in assessing the bactericidal activity of antimicrobial agents and assesses both how much of the original inoculum was killed and the rate of such killing. See p. 142 under "Bactericidal Testing".

It would have been prima facie obvious to one of ordinary skill in the art at the time the instant invention was made to modify the method of the combination of Peck et al and Remacle et al and Taintor et al so as to assess by the said DNA detection method the number of one or more microorganisms in an aliquot at a plurality of time points within the pre-determined or incubation period with antimicrobial in an aliquot, thus resulting in a time kill curve with a reasonable expectation of success. The motivation to do so is taught by Gorbach et al who teach that a time kill curve is a research tool that is used in assessing the bactericidal activity of antimicrobial agents and assesses both how much of the original inoculum was killed and the rate of such killing.

Status of Claims

Claims 1-9, 12-17 and 20 are rejected. No claims allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to OLUWATOSIN OGUNBIYI whose telephone number is (571)272-9939. The examiner can normally be reached on M-F 5:30 am- 2:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Patricia Duffy can be reached on 571-272-0855. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Oluwatosin Ogunbiyi/
Examiner, Art Unit 1645